



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 2

[Docket No. FDA-2015-N-1355]

Use of Ozone-Depleting Substances; Request for Comment Concerning Essential-Use Designations

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice and request for public comment.

SUMMARY: The Food and Drug Administration (FDA or Agency) is seeking public comment on whether the uses of ozone-depleting substances (ODSs), including chlorofluorocarbons (CFCs), in certain FDA-regulated products currently designated essential are no longer essential under the Clean Air Act due to the availability of alternatives that do not use CFCs or because the products are no longer being marketed. Essential-use products are exempt from FDA's ban on the use of CFC propellants in FDA-regulated products and the Environmental Protection Agency's (EPA's) ban on the use of CFCs in pressurized dispensers. FDA is seeking public comment because it is responsible for determining which FDA-regulated products that release CFCs or other ODSs are essential uses under the Clean Air Act. FDA is soliciting comments to assist the Agency in striking an appropriate balance that will best protect the public health, both by ensuring the availability of an adequate number of alternatives and by curtailing the release of ODSs.

DATES: Submit written or electronic comments by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments by any of the following methods:

#### Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

#### Written Submissions

Submit written submissions in the following ways:

- Mail/Hand delivery/Courier (for paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Docket No(s). ([INSERT]). All comments received may be posted without change to <http://www.regulations.gov>, including any personal information provided. For additional information on submitting comments, see the "Comments" heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.regulations.gov> and insert the docket number(s), found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Daniel Orr, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6246, Silver Spring, MD 20993, 240-402-0979, [daniel.orr@fda.hhs.gov](mailto:daniel.orr@fda.hhs.gov).

## SUPPLEMENTARY INFORMATION:

### I. Background

Any drug, device, cosmetic, or food contained in an aerosol product or other pressurized dispenser that releases a CFC or other ODS propellant is not an essential use of the ODS under the Clean Air Act except as provided in 21 CFR 2.125(c) and (e). This prohibition is based on scientific research indicating that CFCs reduce the amount of ozone in the stratosphere and thereby increase the amount of ultraviolet radiation reaching the Earth. An increase in ultraviolet radiation will increase the incidence of skin cancer, and produce other adverse effects of unknown magnitude on humans, animals, and plants. Sections 2.125(c) and (e) provide exemptions for essential uses of ODSs for certain products containing ODS propellants that FDA determines provide unique health benefits that would not be available without the use of a CFC.

EPA regulations implementing the provisions of section 610 of the Clean Air Act (42 U.S.C. 7671i) contain a general ban on the use of CFCs in pressurized dispensers, such as metered-dose inhalers (MDIs) (40 CFR 82.64(c) and 82.66(d)). These EPA regulations exempt from the general ban “medical devices” that FDA considers essential and that are listed in 21 CFR 2.125(e). Section 601(8) of the Clean Air Act (42 U.S.C. 7671(8)) defines “medical device” as any device (as defined in the FD&C Act), diagnostic product, drug (as defined in the FD&C Act), and drug delivery system, if such device, diagnostic product, drug, or drug delivery system uses a class I or class II ODS for which no safe and effective alternative has been developed (and, where necessary, approved by the Commissioner of Food and Drugs (the Commissioner)); and if such device, diagnostic product, drug, or drug delivery system has, after notice and opportunity for public comment, been approved and determined to be essential by the Commissioner in consultation with the Administrator of EPA (the Administrator). Class I

substances include CFCs, halons, carbon tetrachloride, methyl chloroform, methyl bromide, and other chemicals not relevant to this document (see 40 CFR part 82, appendix A to subpart A).

Class II substances include hydrochlorofluorocarbons (see 40 CFR part 82, appendix B to subpart A).

Production of ODSs is being phased out worldwide under the terms of the Montreal Protocol on Substances that Deplete the Ozone Layer (Montreal Protocol), Sept. 16, 1987, S. Treaty Doc. No. 10, 100th Cong., 1st sess., 26 I.L.M. 1541 (1987). In accordance with the provisions of the Montreal Protocol, under authority of Title VI of the Clean Air Act (section 601 et seq.), manufacture of ODSs, including CFCs, in the United States was banned generally as of January 1, 1996. To receive permission to manufacture CFCs in the United States after the phase-out date, manufacturers must obtain an exemption from the phase-out requirements from the Parties to the Montreal Protocol. Procedures for securing an essential-use exemption under the Montreal Protocol are described in the most recent request by EPA for applications for exemptions (60 FR 54349, October 23, 1995). Firms that wish to use CFCs manufactured after the phase-out date in medical devices (as defined in section 601(8) of the Clean Air Act) covered under section 610 of the Clean Air Act must receive exemptions for essential uses under the Montreal Protocol.

Faced with the statutorily mandated phase-out of the production of CFCs, drug manufacturers have developed alternatives to MDIs and other self-pressurized drug dosage forms that do not contain ODSs. Examples of these alternative dosage forms are MDIs that use non-ODSs as propellants and dry-powder inhalers. The current and future availability of technically feasible alternatives to the use of a CFC may mean that the existing listing of an essential use in 21 CFR 2.125(e) no longer reflects current conditions. It is with this situation in mind that FDA

is seeking public comment regarding the Agency's consideration of whether certain uses of ODSs are no longer essential.

FDA is soliciting comments to assist the Agency in striking an appropriate balance that will best protect the public health by ensuring the availability of an adequate number of treatment alternatives and by curtailing the release of ODSs.

## II. Listed Uses That May No Longer Be Considered Essential

There are certain uses of CFCs currently listed in 21 CFR 2.125(e) as essential that may no longer be considered as essential. Section 2.125(g) sets forth standards for determining whether the use of an ODS in a medical product is no longer essential. FDA is seeking public comment concerning whether the following uses should still be considered essential:

### A. Sterile Aerosol Talc Administered Intrapleurally by Thoracoscopy for Human use (21 CFR 2.125(e)(4)(ix))

There is currently one sterile aerosol talc product containing ODSs which is approved for administration intrapleurally by thoracoscopy for human use for the treatment of recurrent malignant pleural effusion (MPE) in symptomatic patients. Under 21 CFR 2.125(g)(3), an essential-use designation for individual active moieties marketed as ODS products and represented by one new drug application may no longer be essential if:

- At least one non-ODS product with the same active moiety is marketed with the same route of administration, for the same indication, and with approximately the same level of convenience of use as the ODS product containing that active moiety;
- Supplies and production capacity for the non-ODS product(s) exist or will exist at levels sufficient to meet patient need;
- Adequate U.S. postmarketing-use data are available for the non-ODS product(s); and

- Patients who medically require the ODS product are adequately served by the non-ODS product(s) containing that active moiety and other available products (21 CFR 2.125(g)(3)).

Sterile aerosol talc is currently marketed for intrapleural administration in two non-ODS formulations--powder and aerosol. Sterile aerosol talc is a powder formulation of talc available for intrapleural administration via chest tube. Sclerosol Intrapleural Aerosol (sterile talc powder) is an aerosol formulation which contains the propellant, hydrofluoroalkane (HFA) 134a and is approved for intrapleural administration. Sclerosol Intrapleural Alcohol, a form of aerosol sterile talc, is indicated for the treatment of recurrent MPE in symptomatic patients.

The route of administration, indications, and level of convenience appear to be the same for the ODS and non-ODS formulations of sterile aerosol talc. Moreover, because production of non-ODS formulations are not limited by restrictions on the use of ODSs, the Agency believes that non-ODS formulations can be produced at greater quantities and have the potential to be more widely available than prior formulations that contained ODSs. In addition, there is adequate U.S. postmarketing-use data indicating that the non-ODS products are available in sufficient quantities to serve the current patient population. For these reasons, we believe that patients may be adequately served by the non-ODS products containing sterile aerosol talc. Thus, FDA is seeking public comment concerning whether sterile aerosol talc administered intrapleurally by thoracoscopy for human use is no longer an essential use of ODSs described in 21 CFR 2.125(e).

#### **B. Drug Products That Are No Longer Being Marketed**

Under 21 CFR 2.125(g)(1), an active moiety may no longer be an essential-use (21 CFR 2.125(e)) if it is no longer marketed in an approved ODS formulation. FDA believes failure to market indicates non-essentiality because the absence of a demand sufficient for even one

company to market the product is highly indicative that the use is not essential.

FDA is seeking public comment as to whether metered-dose atropine sulfate aerosol human drugs administered by oral inhalation (21 CFR 2.125(e)(4)(vi)) and anesthetic drugs for topical use on accessible mucous membranes of humans where a cannula is used for application (21 CFR 2.125(e)(4)(iii)) are no longer essential uses as described at 21 CFR 2.125(e). FDA has information that these products are not currently being marketed in an approved form that releases ODSs, and, under 21 CFR 2.125(g)(1), they may no longer constitute an essential-use. Because these products are no longer being marketed, FDA does not believe that loss of essential use status would not result in any drugs being made unavailable to patients.

### III. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

Dated: June 24, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015-15902 Filed: 6/26/2015 08:45 am; Publication Date: 6/29/2015]